Rec'd PCT/PTC 23 MAR 2005

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 1060/401/PWO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/04162	International filing date *(day/month/year)* 23.09.2003	Priority date *(day/month/year)* 24.09.2002
International Patent Classification (IPC) or both national classification and IPC A61K7/16		
Applicant THE BOOTS COMPANY PLC		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
13.04.2004	03.01.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Paloniemi Legland, R Telephone No. +49 89 2399-7315

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/04162

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-22 as originally filed

Claims, Numbers

1-32 filed with telefax on 29.09.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☒ the claims, Nos.: 33
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2,6-14,18-31
	No:	Claims	1,3-5,15-17,32
Inventive step (IS)	Yes:	Claims	2,6-14,18-21,23,28
	No:	Claims	1,3-5,15-17,22,24-27,29-32
Industrial applicability (IA)	Yes:	Claims	1-32
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:

D13: WO 00/16737 A (MCLAUGHLIN GERALD G) 30 March 2000 (2000-03-30)

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT.

The document D13 discloses a teeth whitening composition comprising "Tinopal PT" and as a bleaching agent potassium chlorate (claims 1,6 and 15). Thus the subject-matter of claims 1,3-5, 15-17 and 32 is not novel.

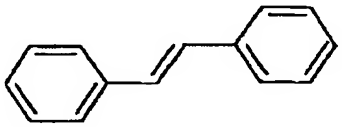
The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 22 does not involve an inventive step in the sense of Article 33(3) PCT.
A sequential application is disclosed in D13 (claim 38) thus being obvious method of administration for a skilled man.
The same reasoning applies, mutatis mutandis, to the subject-matter of the corresponding dependent claims 24-27, which therefore are also considered not inventive.
Dependent claims 29-31 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step. There is no inventive activity needed to let the dentist do the first application of the whitening agent and let the patient do the second application by himself.

Independent claim 2 is directed to a method for whitening the teeth comprising as a fluorescent whitening agent a bis-styrylphenyl compound. This compound is not known from the availbale prior art for a whitening agent of the teeth. Thus the subject-matter of claim 2 is novel. The technical problem was to provide an alternative teeth whitening method and the solution was to use the specific fluorescent whitening compounds. Document D13 as closest prior art discloses a composition for whitening a tooth comprising Tinopal PT (and a bleaching agent). There are no hints in D13 for a skilled man to use bis-styrylbiphenyl compounds (Tinopal CBS; Tinopal CBS-X) for tooth

whitening. Therefre the subject-matter of claim 2 involves an inventive step. The same reasoning applies to the dependent claims 7-14 and 18-21.

Claims

1. A method for improving or enhancing the appearance of the teeth, in particular for whitening of the teeth, which method comprises application to the teeth of a dental composition comprising a fluorescent whitening agent selected from derivatives of stilbene having the following chromophore system:



as the sole tooth whitening agent in the composition, or with one or more additional tooth whitening agents selected from

a) abrasive agents effective in physically removing stains from the tooth enamel;

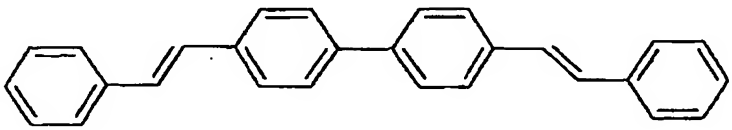
b) chlorite oxidising or bleaching agents;

c) enzymatic systems; and

d) chelating agents;

and a dentally acceptable diluent or carrier.

2. A method for improving or enhancing the appearance of the teeth, in particular for whitening of the teeth, which method comprises application to the teeth of a dental composition comprising a fluorescent whitening agent selected from bis-styrylbiphenyl compounds having the following chromophore system:

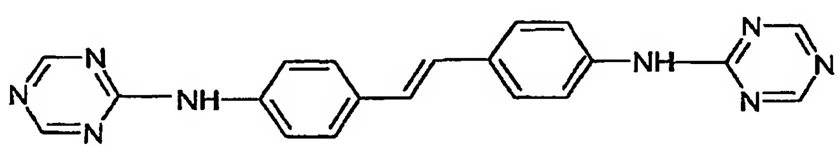


and a dentally acceptable diluent or carrier, optionally with an additional tooth whitening agent.

3. A method as claimed in Claim 1 or Claim 2, wherein the composition is formulated as a toothpaste, mouthrinse, toothgel, tooth paint or dental gel.

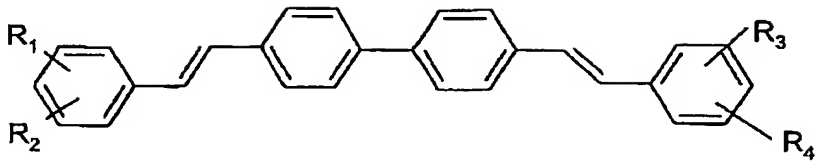
4. A method as claimed in any preceding claim, wherein the fluorescent whitening agent absorbs light of wavelength less than 380nm and re-emits light in the wavelength range 400nm to 450nm.

5. A method as claimed in Claim 1, wherein the fluorescent whitening agent is selected from bis-triazineamine derivatives of compounds having the following chemical backbone:



6. A method as claimed in Claim 1, wherein the fluorescent whitening agent is selected from the group consisting of disodium 4,4'-bis[(4-anilino-6-morpholino-1,3,5-triazin-2-yl)amino]stilbene-2,2'-disulfonate, disodium 4,4'-bis{[4-anilino-6-(N-methyl-N-2-hydroxyethyl)amino-1,3,5-triazin-2-yl] amino}stilbene-2,2'-disulfonate, and disodium 4,4'-bis[(4-anilino-6-methylamino-1,3,5-triazin-2-yl)aminolstilbene-2,2'-disulfonate.

7. A method as claimed in Claim 2, wherein the fluorescent whitening agent is a bis-styrylbiphenyl compound of the general formula:



in which R_1 is $-SO_3M$ and R_2, R_3 and R_4, which may be the same or different, are selected from R_5, $-SO_3M$, halogen (particularly Cl), -CN, $-OC(=O)R_5$, $-COOR_5$, $-SO_2N(R_5)_2$ and $-CON(R_5)_2$, wherein R_5 represents hydrogen or C_{1-8} alkyl and M represents hydrogen or a Group I metal, eg Na, K or Li.

8. A method as claimed in Claim 7, wherein R_3 is the same as R_1, and R_2 and R_4 are the same and are selected from R_5, halogen, -CN, $-OC(=O)R_5$, $-COOR_5$, $-SO_2N(R_5)_2$ and $-CON(R_5)_2$.

9. A method as claimed in Claim 8, wherein the fluorescent whitening agent is 4,4'-bis(2-sulfostyryl)biphenyl or a salt or other soluble derivative thereof.

10. A method as claimed in Claim 9, wherein the fluorescent whitening agent is disodium 4,4'-bis(2-sulfostyryl)biphenyl.

11. A method as claimed in any preceding claim, wherein the concentration of fluorescent whitening agent in the composition is less than 1,000 ppm.

12. A method as claimed in Claim 11, wherein the concentration of fluorescent whitening agent in the composition is in the range 50ppm to 500ppm.

13. A method as claimed in any Claim 11, wherein the concentration of fluorescent whitening agent in the composition is less than 100ppm.

14. A method as claimed in Claim 13, wherein the concentration of fluorescent whitening agent in the composition is in the range 5ppm to 50ppm.

15. A method as claimed in any preceding claim, wherein the method further comprises the application of an additional tooth whitening agent.

16. A method as claimed in Claim 15, wherein application of the additional tooth whitening agent is simultaneous with application of the fluorescent whitening agent.

17. A method as claimed in Claim 15, wherein the composition comprises an additional tooth whitening agent.

18. A method as claimed in Claim 2, wherein the composition comprises a bleaching agent as an additional tooth whitening agent.

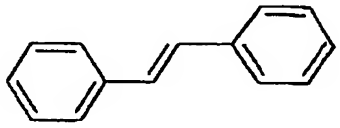
19. A method as claimed in Claim 18, wherein the bleaching agent is a peroxide.

20. A method as claimed in Claim 19, wherein the peroxide is hydrogen peroxide or a compound that generates hydrogen peroxide in use.

21. A method as claimed in Claim 18, wherein the bleaching agent is a chlorite bleaching agent.

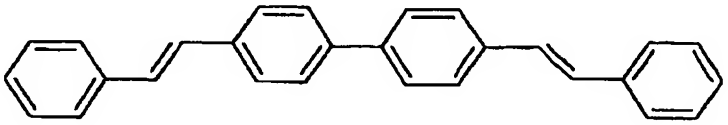
22. A method for improving or enhancing the appearance of the teeth, in particular for whitening of the teeth, which method comprises application to

the teeth of a dental composition comprising a fluorescent whitening agent selected from the group consisting of derivatives of stilbene having the following chromophore system:



and an additional tooth whitening agent wherein the method comprises the sequential application to the teeth of the additional tooth whitening agent followed by the fluorescent whitening agent.

23. A method as claimed in claim 22, wherein the fluorescent whitening agent compounds have the following chromophore system:



24. A method as claimed in Claim 22 or Claim 23, wherein the additional tooth whitening agent is a bleaching agent.

25. A method as claimed in Claim 24 wherein the bleaching agent is a peroxide.

26. A method as claimed in Claim 25, wherein the peroxide is hydrogen peroxide or a compound that generates hydrogen peroxide in use.

27. A method as claimed in any one of claims 22 to 26, wherein one or more applications of the additional tooth whitening agent precede application of the fluorescent whitening agent.

28. A method as claimed in any one of claims 22 to 27, wherein the fluorescent whitening agent is selected from the group consisting of disodium 4,4'-bis(2-sulfostyryl)biphenyl, 4,4'-bis(2-sulfostyryl)biphenyl, disodium 4,4'-bis(3-sulfo-4-chlorostyryl)biphenyl, disodium 4,4'-bis[(4-anilino-6-morpholino-1,3,5-triazin-2-yl)amino]stilbene-2,2'-disulfonate, disodium 4,4'-bis{[4-anilino-6-(N-methyl-N-2-hydroxyethyl)amino-1,3,5-triazin-2-yl] amino}stilbene-2,2'-disulfonate, and disodium 4,4'-bis[(4-anilino-6-methylamino-1,3,5-triazin-2-yl)aminolstilbene-2,2'-disulfonate.

29. A method as claimed in any one of Claims 22 to 28, comprising a first stage in which the additional tooth whitening agent is applied by a dental surgeon, and a second stage in which the fluorescent whitening agent and the additional tooth whitening agent are applied, simultaneously or sequentially, by the patient.

30. A method as claimed in Claim 29, wherein in the first stage the additional tooth whitening agent is applied first, followed by a fluorescent whitening agent.

31. A method as claimed in Claim 28 or Claim 29, wherein in the second stage, the additional tooth whitening agent and the fluorescent whitening agent are applied simultaneously.

32. A method for improving or enhancing the appearance of the teeth, in particular for whitening of the teeth, substantially as hereinbefore described.

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